

## CLAIMS

1. A method for altering a B cell mediated pathology in a patient, said method comprising:

administering a composition comprising a chimeric protein;

5 said chimeric protein comprising at least a portion of a V<sub>H</sub> or V<sub>L</sub> region and at least a portion of an immunoglobulin constant region;

wherein said V<sub>H</sub> or V<sub>L</sub> region is associated with a B cell clone from said patient having said B cell mediated pathology;

10 and said administering of said composition alters said B cell mediated pathology in said patient.

2. The method of claim 1 wherein said composition further comprises a second chimeric protein that comprises at least a portion of V<sub>H</sub> or V<sub>L</sub> region and at least a portion of a second immunoglobulin constant region.

3. The method of claim 1 wherein said immunoglobulin constant region  
15 comprises a human IgG<sub>γ1</sub> constant region.

4. The method of claim 1 wherein said V<sub>H</sub> or V<sub>L</sub> region is a V<sub>H</sub> region.

5. The method of claim 1 wherein said V<sub>H</sub> or V<sub>L</sub> region is a V<sub>L</sub> region.

6. The method of claim 1 or 2 wherein said V<sub>H</sub> or V<sub>L</sub> region of said first chimeric protein comprises a V<sub>H</sub> region and said second chimeric protein comprises a  
20 V<sub>L</sub> region.

7. The method of claim 2 wherein said second immunoglobulin constant region comprises a human  $\kappa$  or  $\lambda$  constant region.

8. The method of claim 1 or 2 wherein said  $V_H$  or  $V_L$  region is an entire variable region.

5 9. The method of claim 1 or 2 wherein said  $V_L$  region is an entire variable region.

10 10. The method of claim 1 or 2 wherein said first or second immunoglobulin constant region is selected from the group consisting of a human  $IgG_{\gamma 1}$  constant region, a human  $IgG_{\gamma 2}$  constant region, a human  $IgG_{\gamma 3}$  constant region, a human  $IgG_{\gamma 4}$  constant region, a human  $IgA_1$  constant region, a human  $IgA_2$  constant region, a human  $IgM$  constant region, a human  $IgD$  constant region, a human  $IgE$  constant region, a human  $\kappa$  chain constant region, and a human  $\lambda$  chain constant region.

11. The method of claim 1 wherein said chimeric protein is produced by a method comprising:

15 isolating a gene encoding at least a portion of a  $V_H$  or  $V_L$  region from B cells of said patient having said B cell mediated pathology;

inserting said gene encoding said  $V_H$  or  $V_L$  region and a gene encoding at least a portion of said immunoglobulin constant region into an expression vector to allow the expression of said first chimeric protein;

20 producing said chimeric protein by introducing said expression vector into insect cell lines; and

isolating said chimeric protein.

12. The method of claim 11 further comprising the step of inserting a gene encoding at least a portion of a V<sub>H</sub> or V<sub>L</sub> region and a gene encoding at least a portion of a second immunoglobulin constant region into said expression vector to allow the expression of said second chimeric protein.

5 13. The method of claim 11 or 12 further comprises a step of conjugating said chimeric protein to a carrier protein.

14. The method of claim 13 wherein said carrier protein is keyhole-limpet hemocyanin (KLH).

10 15. The method of claim 1 wherein said composition is further co-administered with a cytokine or chemokine.

16. The method of claim 15 wherein said cytokine is granulocyte-macrophage-colony stimulating factor (GM-CSF).

17. The method of claim 15 wherein said chemokine is monocyte chemotactic protein 3 (MCP-3).

15 18. The method of claim 11 wherein said expression vector is a baculovirus expression vector.

19. The method of claim 18 wherein said baculovirus expression vector comprises a honey bee melittin secretory signal sequence and a human placental alkaline phosphatase secretory signal sequence.

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20. The method of claim 19 wherein said baculovirus expression vector further comprises a baculovirus AcNPV p10 promotor and AcNPV polyhedrin promotor, wherein said p10 promotor controls a honey bee melittin secretory signal sequence, and wherein said polyhedrin promotor controls a human placental alkaline phosphatase secretory signal sequence.

21. The method of claim 20 wherein a gene encoding a chimeric protein comprising a  $V_H$  region and a first immunoglobulin constant region is controlled by said p10 promotor in said baculovirus expression vector, a gene encoding a chimeric protein comprising a  $V_L$  region and a second first immunoglobulin constant region is controlled by polyhedrin promotor in said baculovirus expression vector.

22. The method of claim 20 wherein said gene comprising said  $V_H$  or  $V_L$  region and said gene encoding said immunoglobulin constant region is controlled by either said p10 promotor or polyhedrin promotor in said baculovirus expression vector.

23. The method of claim 11 wherein said gene encoding said immunoglobulin constant region is a human  $IgG_{\gamma 1}$  gene.

24. The method of claim 12 wherein said gene encoding said second immunoglobulin constant region is a gene encoding for a human  $\kappa$  or  $\lambda$  constant region.

25. The method of claim 11 or 12 wherein said gene encoding said immunoglobulin constant region is selected from the group consisting of a human  $IgG_{\gamma 1}$  constant region, a human  $IgG_{\gamma 2}$  constant region, a human  $IgG_{\gamma 3}$  constant region, a human  $IgG_{\gamma 4}$  constant region, a human  $IgA_1$  constant region, a  $IgA_2$  human constant

region, a human IgM constant region, a human IgD constant region, a human IgE constant region, a human  $\kappa$  chain constant region, and a human  $\lambda$  chain constant region.

26. The method of claim 11 wherein said chimeric protein is selected from the group consisting of a protein comprising said  $V_H$  region and a human IgG $_{\gamma 1}$  constant region; a protein comprising said  $V_L$  region and a human  $\kappa$  chain constant region; and a protein comprising said  $V_L$  region and a human  $\lambda$  chain constant region.

27. The method of claim 12 wherein said first and second chimeric proteins comprise a protein comprising said  $V_H$  region and a human IgG $_{\gamma 1}$  constant region and a protein comprising said  $V_L$  region and a human  $\kappa$  or  $\lambda$  chain constant region.

28. The method of claim 11 wherein said insect cell lines are *Trichoplusia ni* (*Hi - 5*) or *Spodoptera frugiperda* (*sf9*) cell lines.

29. The method of claim 11 or 12 wherein said chimeric proteins are analyzed for expression by ELISA.

30. The method of claim 11 or 12 wherein said chimeric proteins are isolated using a protein selected from the group consisting of protein A, protein G, protein L and other proteins being able to bind to an immunoglobulin binding domain.

31. The method of claim 30 wherein said other protein able to bind an immunoglobulin binding domain is an anti-immunoglobulin antibody.

32. The method of claim 1 wherein said B cell mediated pathology is a B cell lymphoma.

33. The method of claim 32 wherein said B cell lymphoma is refractory low grade lymphoma or follicular B cell lymphoma.

34. A composition for altering a B cell mediated pathology in a patient comprising:

5 a chimeric protein that comprises at least a portion of a  $V_H$  or  $V_L$  region linked to at least a portion of an immunoglobulin constant region, wherein said  $V_H$  or  $V_L$  region is associated with a B cell clone from said patient having said B cell mediated pathology.

10 35. A composition of claim 34 further comprising a second chimeric protein that comprises at least a portion of a variable region of a  $V_H$  or  $V_L$  region and at least a portion of a second immunoglobulin constant region, wherein said variable region is associated with a B cell clone from said patient having said B cell mediated pathology.

36. The composition of claim 34 or 35 wherein said chimeric proteins are produced in according to claim 13 or 14.

15 37. The composition of claim 34 or 35 wherein said immunoglobulin constant regions are selected from the group consisting of a human  $IgG_{\gamma 1}$  constant region, a human  $IgG_{\gamma 2}$  constant region, a human  $IgG_{\gamma 3}$  constant region, a human  $IgG_{\gamma 4}$  constant region, a human  $IgA_1$  constant region, a human  $IgA_2$  constant region, a human  $IgM$  constant region, a human  $IgD$  constant region, a human  $IgE$  constant region, a  
20 human  $\kappa$  chain constant region, and a human  $\lambda$  chain constant region.

38. The composition of claim 34 wherein said immunoglobulin constant region is a human  $IgG_{\gamma 1}$  constant region operatively linked to said  $V_H$  region.

39. The composition of claim 34 wherein said immunoglobulin constant region is a human  $\kappa$  or  $\lambda$  constant region operatively linked to said  $V_L$  region.

40. The composition claim 35 wherein said first and second chimeric proteins are said  $V_H$  region operatively linked to a human  $IgG_{\gamma 1}$  constant region and said  
5  $V_L$  region operatively linked to a human  $\kappa$  or  $\lambda$  constant region.

41. The composition of claim 34 or 35 further comprises a carrier protein.

42. The composition of claim 41 wherein said carrier protein is keyhole-limpet hemocyanin (KLH).

43. The composition of claim 34 or 35 is further co-administered with a  
10 cytokine or chemokine.

44. The composition of claim 43 wherein said cytokine is granulocyte-macrophage-CSF.

45. The composition of claim 43 wherein said chemokine is a monocyte chemotactic protein 3 (MCP 3).

46. The composition of claim 34 or 35 wherein said composition is a  
15 vaccine.

47. The composition of claim 34 wherein said B cell mediated pathology is a B cell lymphoma.

48. The composition of claim 47 wherein said B cell lymphoma is non-Hodgkins lymphoma.

49. The composition of claim 47 wherein said B cell lymphoma is refractory low grade or follicular B cell lymphoma.

50. The composition of claim 34 is further administered by injection, inhalation, oral or transdermal delivery.

51. The composition of claim 34 wherein said B cell mediated pathology is an autoimmune disease selected from the group consisting of multiple sclerosis, systemic lupus erythematosus, anti-Hu associated paraneoplastic neurological syndrome, autoimmune hepatitis, Type I diabetes, autoimmune thyroiditis, and scleroderma.

52. An expression vector comprising (a) a chimeric gene encoding a portion of a V<sub>L</sub> region and a portion of a gene encoding a κ light chain, both operatively linked to a human placental alkaline phosphatase secretory signal sequence and a polyhedrin promoter, and (b) a chimeric gene encoding a portion of a V<sub>H</sub> region and a portion of an IgG<sub>1</sub> heavy chain, both operatively linked to a honey bee melittin secretory signal sequence and a P10 promoter.

53. A baculovirus expression vector comprising (a) a chimeric gene encoding a portion of a V<sub>L</sub> region and a portion of a gene encoding a κ light chain, both operatively linked to a human placental alkaline phosphatase secretory signal sequence and a polyhedrin promoter, and (b) a chimeric gene encoding a portion of a V<sub>H</sub> region and a portion of an IgG<sub>1</sub> heavy chain, both operatively linked to a honey bee melittin secretory signal sequence and a P10 promoter.



54. An expression vector comprising (a) a portion of a gene encoding a  $\kappa$  light chain constant region operatively linked to a human placental alkaline phosphatase secretory signal sequence and a polyhedrin promoter, and (b) a portion of a gene  
5 encoding an IgG<sub>1</sub> heavy chain constant region operatively linked to a honey bee melittin secretory signal sequence and a P10 promoter.

55. An expression vector comprising (a) a portion of a gene encoding a  $\lambda$  light chain constant region operatively linked to a human placental alkaline phosphatase  
10 secretory signal sequence and a polyhedrin promoter, and (b) a portion of a gene encoding an IgG<sub>1</sub> heavy chain constant region operatively linked to a honey bee melittin secretory signal sequence and a P10 promoter.

56. A vector comprising the nucleic acid sequence as set forth in SEQ ID  
15 NO:6.

57. A vector comprising the nucleic acid sequence as set forth in SEQ ID  
NO:7.

58. A vector comprising the nucleic acid sequence as set forth in SEQ ID  
20 NO:89.

59. A vector comprising the nucleic acid sequence as set forth in SEQ ID  
NO:90.

25

60. A vector comprising the nucleic acid sequence as set forth in SEQ ID  
NO:91.